# POSTOPERATIVE RESIDUAL NEUROMUSCULAR BLOCK

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Almost 60 years ago the use neuromuscular blocking agents (NMBA) was associated with significantly increased risk of perioperative (approx. 6 fold) mortality (1). However, recent achievements in monitoring conditions and in synthesis of new drugs provided a safety margin of the use of NMBA`s. Quantitative and qualitative neuromuscular monitoring devices and understanding of the importance of monitoring allows more accurate dosing and titration of NMBA in the perioperative period. The optimization of NMBA during surgery not only increases the comfort of the surgeon leading more successful and satisfactory outcome, but also decreases the incidence of critical events such as hypoxia, carbon dioxide retention, muscle weakness, blurred vision, difficulty in mobilization and prolonged stay at Postoperative Anesthesia Care Unit (PACU) or Intensive Care Units (2).

## Definition of Residual Neuromuscular Block

In the early 70`s the concept of neuromuscular monitoring was introduced to the clinical practice. Train of four was defined as four supra maximal stimuli delivered every 0.5 seconds (2Hz) and the muscle response to the fourth stimulus is compared with that of the first stimulus. Basically the degree of fade closely correlates to the degree of block. According to the previous data the threshold for recovery of block was defined as TOF > 0.7 (4). It was believed that patients with higher TOF ratio of 0.7 were capable of opening their eyes widely, coughing, protruding the tongue, sustaining head lift for 5 seconds, developing a forced vital capacity of at least 15 to

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20 mL/kg and sustaining titanic stimulation without fade for 5 seconds (5, 6). However more recent data showed that patients with TOF ratio less than 0.9 are more prone to have pharyngeal dysfunction and an increased risk of aspiration (7). According to the new and recent understanding the new threshold is set to TOF>0.9. On the other hand the threshold means clinically not too much as clinical signs should also be adapted to every clinician`s daily practice.

## The Incidence of Residual Block



The incidence of residual block differs widely due to the patient population, type of the surgery, the method used to assess the block, the objective and subjective criteria and the preferred agent (long , intermediate or short acting) (8). There is a considerable amount of patients with residual block even after a single intubating dose of vecuronium (42% TOF < 0.7). Moreover the incidence is also terrifying even in outpatient population compared inpatients (38% vs 47%) (10). It was also clearly demonstrated that the clinical signs such as capable of opening their eyes widely, coughing, protruding the tongue, sustaining head lift for 5 seconds, developing a forced vital capacity of at least 15 to 20 mL/kg are not reliable criteria to predict actual neuromuscular block (Figure 1). Naguib et al carried out a meta analysis for the incidence of residual neuromuscular block and reported the incidence with TOF < 0.9 as 41% (11). According these data the postoperative residual neuromuscular block is a common clinical problem but unfortunately it is a bit underestimated by the clinicians. The data are conflicting due to different methodology and especially the different NMBAs (Figure 2).

**Table 3.** Diagnostic Attributes of the Clinical Tests; Sensitivity, Specificity, Positive and Negative Predictive Values of an Individual Clinical Test for a Train-of-Four <90%

| Variable | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
|---|---|---|---|---|
| Inability to smile | 0.29 | 0.80 | 0.47 | 0.64 |
| Inability to swallow | 0.21 | 0.85 | 0.47 | 0.63 |
| Inability to speak | 0.29 | 0.80 | 0.47 | 0.64 |
| General weakness | 0.35 | 0.78 | 0.51 | 0.66 |
| Inability to lift head for 5 s | 0.19 | 0.88 | 0.51 | 0.64 |
| Inability to lift leg for 5 s | 0.25 | 0.84 | 0.50 | 0.64 |
| Inability to sustained hand grip for 5 s | 0.18 | 0.89 | 0.51 | 0.63 |
| Inability to perform sustained tongue depressor test | 0.22 | 0.88 | 0.52 | 0.64 |

The sensitivity of a test is the number of true positives divided by the sum of true positives + false negatives; the specificity is the number of true negatives divided by the sum of true negatives + false positives. True positives are patients scoring positive for a test and having a train-of-four (TOF) <90%. False negatives are patients with a negative test result but a TOF <90%. True negatives have a negative test score and a TOF not <90% false positives score positively but have a TOF not <90%. A *positive* test result means *inability* to smile, swallow and speak, general muscular weakness, etc.

**Figure 1.** *The clinical tests are not reliable predictors of actual neuromuscular block. (Cammu G, De Witte J, De Veylder J, Byttebier G, Vandeput D, Foubert L, Vandenbroucke G, Deloof T. Postoperative residual paralysis in outpatients versus inpatients. Anesth Analg 2006;102:426–9)*

**Table 1. Incidence of Residual Neuromuscular Blockade (2000–2008)**

| Author | Year | Number of patients | NMBD used | NM monitoring used (%) | Reversal used (%) | Site/time RNMB measured | Definition RNMB | Incidence RNMB | Type of anesthesia |
|---|---|---|---|---|---|---|---|---|---|
| Baillard et al.[27] | 2000 | 568 | Vecuronium | 2 | 0 | PACU | <0.7 | 42% (AMG) | Inhalational |
| Blissinger et al.[20] | 2000 | 83 | Pancuronium | NS | 100 | PACU | <0.7 | 20% (AMG) | Inhalational and TIVA |
| | | | Vecuronium | NS | 100 | PACU | <0.7 | 7% | |
| Hayes et al.[22] | 2001 | 148 | Vecuronium | 41 | 88 | PACU | <0.8 | 64% (AMG) | Primarily inhalational |
| | | | Atracurium | 41 | 88 | PACU | <0.8 | 52% | |
| | | | Rocuronium | 41 | 88 | PACU | <0.8 | 39% | |
| McCaul et al.[28] | 2002 | 40 | Atracurium | 50 | 100 | Extubation | <0.7 | 65% (MMG) | NS |
| Kim et al.[2] | 2002 | 602 | Vecuronium | 0 | 100 | PACU | <0.7 | 24.7% (AMG) | Inhalational |
| | | | Rocuronium | 0 | 100 | PACU | <0.7 | 14.7% | |
| Gatke et al.[29] | 2002 | 60 | Rocuronium | 0 | 100 | Extubation | <0.8 | 16.7% (MMG) | TIVA |
| Baillard et al.[21] | 2005 | 101 | Rocuronium | 45 | 43 | PACU | <0.9 | 9% (AMG) | Inhalational |
| | | | Vecuronium | 45 | 43 | PACU | <0.9 | 9% | Inhalational |
| Debaene et al.[3] | 2003 | 526 | Vecuronium | NS | 0 | PACU | <0.7 | 16% (AMG) | Inhalational |
| | | | Rocuronium | NS | 0 | PACU | <0.9 | 45% | Inhalational |
| | | | Atracurium | NS | 0 | PACU | | | |
| Baillard et al.[21] | 2005 | 218 | Vecuronium | 60 | 42 | PACU | <0.9 | 3.5% (AMG) | Inhalational |
| | | | Atracurium | 60 | 42 | PACU | <0.9 | 3.5% | Inhalational |
| Kopman et al.[24] | 2004 | 60 | Cisatracurium | 100 | 100 | Transfer to | <0.9 | 36.7% (MMG) | Inhalational |
| | | | Rocuronium | 100 | 100 | PACU | <0.9 | 50.0% | Inhalational |
| Murphy et al.[26] | 2004 | 70 | Pancuronium | 100 | 100 | PACU | <0.9 | 83% (AMG) | Inhalational |
| | | | Rocuronium | 100 | 100 | PACU | <0.9 | 29% | Inhalational |
| Murphy et al.[25] | 2005 | 120 | Rocuronium | 100 | 100 | Extubation | <0.9 | 88% (AMG) | Inhalational |
| Cammu et al.[4] | 2006 | 640 | Atracurium | 11–12 | 25–26 | PACU | <0.9 | 38–47% (AMG) | NS |
| | | | Mivacurium | 11–12 | 25–26 | PACU | <0.9 | 38–47% | NS |
| | | | Rocuronium | 11–12 | 25–26 | PACU | <0.9 | 38–47% | NS |
| Maybauer et al.[29] | 2007 | 339 | Cisatracurium | 100 | 0 | Extubation | <0.9 | 57% (AMG) | TIVA |
| | | | Rocuronium | 100 | 0 | Extubation | <0.9 | 44% | TIVA |
| Murphy et al.[6] | 2008 | 90 | Rocuronium | 100 | 100 | PACU | <0.9 | 30% (AMG) (TOF group) | Inhalational |

NMBD = neuromuscular blocking drugs; NM monitoring= neuromuscular monitoring; RNMB = residual neuromuscular blockade; TIVA = total intravenous anesthesia; NS = not stated.

**Figure 2.** *Incidence of Residuel Neuromuscular Blockade. (Murphy GS, Brull SJ. Residual neuromuscular block: Lessons Unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. Anesth Analg 2010; 111: 120-128)*

## Factors Influencing The Incidence of Postoperative Residual Neuromuscular Blockade

There are several factors playing role on the postoperative residual neuromuscular blockade. In other words the residual block is multifactorial (8).

1. Definition of residual neuromuscular blockade,
   Objective TOF measurements (TOF ratio < 0.7, 0.8, or 0.9),
   Clinical signs or symptoms of muscle weakness
2. Method of objective measurement of residual neuromuscular blockade
   Mechanomyography (MMG) "Gold Standard"
   Electromyography (EMG)
   Acceleromyography (AMG)
   Kinemyography (KMG)
   Phonomyography (PMG
3. Time of measurement of residual neuromuscular blockade
   Immediately before tracheal extubation
   Immediately after tracheal extubation
   On arrival to PACU

4. Type and dose of NMBD administered intraoperatively
    Intermediate-acting NMBD
    Long-acting NMBD
5. Use of neuromuscular monitoring intraoperatively
    Qualitative monitoring (TOF and DBS studied)
    Quantitative monitoring (acceleromyography studied)
    No neuromuscular monitoring (clinical signs)
6. Degree of neuromuscular blockade maintained intraoperatively
    TOF count of 1–2
    TOF count of 2–3
7. Type of anesthesia used intraoperatively
    Inhalational drugs
    TIVA
8. Type and dose of anticholinesterase reversal drug
    Neostigmine
    Pyridostigmine
    Edrophonium
9. Duration of anesthesia
10. Time interval between anticholinesterase administration and objective TOF measurements.
11. Patient factors: metabolic derangements in the PACU (acidosis, hypercarbia, hypoxia, and hypothermia)
12. Drug therapy in PACU: opioids, antibiotics

(TOF = train-of-four; PACU = postanesthesia care unit; NMBD = neuromuscular blocking drug; DBS = double-burst stimulation; TIVA = total intravenous anesthesia.)



## Adverse Effects of Residual Neuromuscular Block

The most crucial issue for the residual block is that it may be associated with several clinical situations. There several studies regarding the adverse effects of neuromuscular block and the studies divided into two due to subjects (Volunteer studies vs Clinical studies in surgical patients). The results of different studies were summarized by Murphy and Brull (8).

**Volunteer studies**

Impairment of pharyngeal coordination and force of contraction (MMG TOF ratio 0.8)

Swallowing dysfunction/delayed initiation of the swallowing reflex (MMG TOF ratio 0.8)

Reductions in upper esophageal sphincter tone (MMG TOF ratio 0.9)

Increased risk of aspiration (MMG TOF ratio 0.8)
Reductions in upper airway volumes (AMG TOF ratio 0.8)
Impairment of upper airway dilator muscle function (AMG TOF ratio 0.8)
Decreased inspiratory air flow (AMG TOF ratio 0.8)
Upper airway obstruction (AMG TOF ratio 0.8)
Impaired hypoxic ventilatory drive (MMG TOF ratio 0.7)
Profound symptoms of muscle weakness (visual disturbances, severe facial weakness, difficulty speaking and drinking, generalized weakness (AMG TOF ratios 0.7–0.75)

**Clinical studies in surgical patients**



Increased risk of postoperative hypoxemia (AMG TOF ratio < 0.9)
Increased incidence of upper airway obstruction during transport to the PACU (AMG TOF ratio < 0.9)
Higher risk of critical respiratory events in the PACU (AMG TOF < ratio _0.9)
Symptoms and signs of profound muscle weakness (pancuronium versus rocuronium)
Delays in meeting PACU discharge criteria and achieving actual discharge (AMG TOF ratio < 0.9)
Prolonged postoperative ventilatory weaning and increased intubation times (cardiac surgical patients) (AMG TOF ratio < 0.9)
Increased risk of postoperative pulmonary complications (atelectasis or pneumonia) (MMG TOF ratio < 0.7)

## Methods to reduce the risk of Residual Neuromuscular Blockade

The residual neuromuscular block is a real clinical problem which has a negative impact on the patient outcome. Every effort should be taken in to consideration to reduce the incidence of residual block. The use of long acting NMBAs leads more often residual neuromuscular block. The same clinical profile of long acting NMBAs can be achieved by repeated doses of intermediate NMBAs. The appropriate monitoring and understanding of the pharmacology of NMBAs will help to reduce the incidence. On the other hand, the residual block incidence is still high with intermediate acting NMBAs if the objective monitoring conditions were not used (12). The use of objective monitoring significantly reduces the incidence and increases the patient safety. However routine reversal of neuromuscular blockade is still controversial. The new reversal agent for steroidal NMBAs, sugammadex, provides huge opportunities for almost all patients (12).

## Conclusion

The appropriate understanding of the effects of the neuromuscular blocking agents will provide a more safe practice. The objective monitoring of the blockade will improve the patient outcome.



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